

### **REMARKS**

Favorable consideration and allowance are respectfully requested for claims 1-5 and 9-15 in view of the following remarks.

The Office Action dated October 24, 2003, (the "Office Action") is a 14-way supplemental restriction requirement. The Office Action indicates that this supplemental restriction is appropriate and necessary in view of the allegedly complex subject matter of the claims and the extensive searching required to identify prior art.

Responsive to the restriction requirement, Applicant hereby provisionally elects Group I, Claims 1-3 and 9-15. This provisional election is made with traverse, it being submitted that the structures (sequences) of the individual genes are included in the sequence of the entire cluster, and that the search for prior art relating to the entire cluster will necessarily include the sequences of the individual genes. Applicant respectfully requests reconsideration and withdrawal of the restriction requirement under 37 C.F.R. § 1.143.

The Examiner appears to have misinterpreted the teachings of the present invention as a whole. While it is true that the primary function of the individual genes is to encode individual enzymes, it should also be considered that the primary function of the entire gene cluster (which comprises these individual genes) is to encode a series of individual enzymes, leading to a stepwise building of aclacinomycins. The gene cluster does not simply "produce aclacinomycin" as indicated by the Examiner, rather the individual genes included in the cluster construct aclacinomycin piece-by-piece. Therefore, it does not follow that each of the genes should be separated as an individual invention.

The Examiner appears to believe that "aclacinomycin" is one single compound produced by the gene cluster. This is not the case. The aclacinomycins include a large group of compounds sharing the same aglycone structure (aklavinone) attached to different sugar moieties. Many of the genes

included in the present cluster are involved in the glycosylation portion of aclacinomycin biosynthesis (see page 16, lines 8-11 of the specification). See also page 12, lines 1-2 indicating the “suggested functions of the genes match well with the proposed biosynthetic pathway of sugars of aclacinomycins (Fig. 3).” Figure 3 describes the proposed biosynthesis pathway for sugars found in aclacinomycins. Therefore, use of this cluster (or the individual genes included therein) enables one to modify the sugar moiety of aclacinomycins, and produce anthracycline compounds.

Therefore, just as the structure of the individual genes are inherently included in the sequence of the entire cluster, the primary functions of each and every one of the individual genes are inherently included in the primary function of the entire cluster. Thus, the individual genes (nucleotide sequences) included in the cluster, and combinations of these genes, as well as the entire cluster share a common feature being useful in generating hybrid anthracyclines (aclacinomycins) and, especially, in modifying the sugar moieties of aclacinomycins (see page 3, lines 20-21 of the specification).

For the foregoing reasons, this Supplemental Restriction Requirement violates the unity of invention requirements under the PCT because of the common properties shared by the polynucleotides in the cited groups. Reconsideration and withdrawal of the Supplemental Restriction Requirement is respectfully requested.

### CONCLUSION

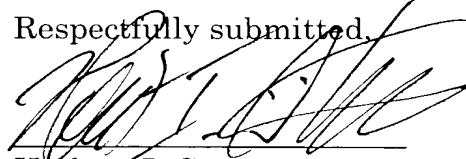
In view of the foregoing, the application is respectfully submitted to be in condition for allowance, and prompt favorable action thereon is earnestly solicited.

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If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket No. 029381.49884US).

Respectfully submitted,



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